REMARKS

Applicants respectfully requests entry of the amendments and remarks submitted herein. Claims 1-56 have been canceled without prejudice to continued prosecution. New claims 57-96 have been added. New claims 57-96 correspond essentially to original claims 32-47 elected in the Response to Restriction Requirement of November 21, 2003. Each new independent claim, however, now recites at least one specific primer or probe sequence. Therefore, support for new claims 57-96 can be found in the originally filed claims and throughout the specification. Reconsideration of the pending application is respectfully requested.

In the Specification

The disclosure stands objected to because the Examiner indicated that it contains embedded hyperlinks and/or other forms of browser-executable code, and that Table 1 contains sequences that are not identified.

Applicants have amended the paragraphs bridging pages 23-24 and 25-26 to remove the hyperlinks. In the Response to Notice to Comply filed June 13, 2002, Applicants amended Table 1 to incorporate sequence identifiers. In view of the previous amendments and the amendments herein, Applicants respectfully request that the objections to the specification be withdrawn.

The 35 U.S.C. §112 Rejections

Claims 32, 35-38, 41-43, 46, and 47 stand rejected under 35 U.S.C. §112, first paragraph, as the Examiner asserted that those claims fail to comply with the written description requirement. This rejection is respectfully traversed.

Without acquiescing to the Examiner's rejection, Applicants have canceled claims 32-47 and submitted new claims 57-96. New claims 57-96 incorporate at least one primer or probe sequence recited in original claims 33, 34, 39, 40, 44, and 45. Since original claims 33, 34, 39, 40, 44, and 45 were not rejected for failing to comply with the written description requirement, new claims 57-96 also should not be rejected for failing to comply with the written description requirement. Applicants respectfully submit that the rejection of claims 32, 35-38, 41-43, 46 and

47 under 35 U.S.C. §112, first paragraph, is moot, and should not be applied to new claims 57-96.

The 35 U.S.C. §103 Rejections

Claims 32, 36-38, 42, 43, and 47 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ramisse et al. (*FEMS Microbiology Letters*, 145:9-16, 1996), Wittwer et al. (*Biotechniques*, 22:130-138, 1997) and Qi et al. (*Appl. Env. Microbiol.*, 67:3720-3727, 2001). Applicants respectfully traverse this rejection.

With respect to the Examiner's statements on page 5 of the Office Action regarding claim interpretation, Applicants do not agree with the Examiner. To expedite prosecution, however, Applicants have canceled claims 32-47 without prejudice to continued prosecution and have submitted new claims 57-96. New claims 57-96 incorporate at least one primer or probe sequence recited in original claims 33, 34, 39, 40, 44, and 45. Applicants respectfully submit that the rejection of claims 32, 36-38, 42, 43, and 47 under 35 U.S.C. §103 is moot. Since original claims 33, 34, 39, 40, 44, and 45 were not rejected over Ramisse et al., Wittwer et al., and Qi et al., this rejection should not be applied to new claims 57-96.

Claims 33-35 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ramisse et al., Wittwer et al., and Qi et al., further in view of Makino et al. (*J. Bacteriol.*, 171:722-30, 1989) and Buck et al. (*Biotechniques*, 27:528-36, 1999). Applicants respectfully traverse this rejection.

With respect to the Examiner's statements on page 5 of the Office Action regarding claim interpretation, Applicants do not agree with the Examiner. To expedite prosecution, however, Applicants have canceled claims 32-47 without prejudice to continued prosecution and have submitted corresponding new claims 57-96. New claims 57-69 and claim 96 recite at least one *capB* primer or probe sequence from original claims 33-35.

The Examiner asserted that the claimed *capB* primers and probes are "structural homologs derived from sequences suggested by the prior art," and cited *In re Deuel* to support this assertion. The Examiner relied, in part, on Makino et al., which discloses the sequence of

capB, and Buck et al., which discloses that a number of different sequencing primers all were used successfully to sequence a particular target nucleic acid.

The claimed *capB* primers and probes are not "structural homologs" of the *capB* sequence disclosed by Makino et al. *In re Deuel* does not indicate that primer and/or probe sequences complementary to a target sequence are "structural homologs." *In re Deuel* is not relevant to the pending claims reciting particular primer or probe sequences, as *In re Deuel* dealt with the obviousness of nucleic acid sequences over prior art references that disclosed an amino acid sequence (or a partial amino acid sequence) encoded by such nucleic acid sequences. Applicant is aware of no case law standing for the proposition that a longer sequence makes *per se* obvious specific primer and probe sequences from within that longer sequence.

There is no suggestion by Makino et al. to select the claimed primers and probes from the entire *capB* sequence. In addition, the results of Buck et al. were not based on amplification of *capB* nucleic acid sequences, and were not even based on amplification of *B. anthacis* nucleic acid sequences. Buck et al. compared sequencing primers using rhodamine or dichlororhodamine dye terminators in automated sequencing reactions. Even ignoring the fact that Buck et al. does not use *B. anthracis* nucleic acids, an automated sequencing reaction is significantly different than, for example, PCR in which, generally, at least two oligonucleotides are used, or real-time PCR in which, generally, at least four oligonucleotides are used. Applicants submit that the results reported by Buck et al. using sequencing primers are not representative of results using different primer and probe sequences in various types of amplification reactions. See, for example, the guidelines published by the University of Chicago Cancer Research Center DNA Sequencing Facility (cancer-seqbase.uchicago.edu/primers/html on the World Wide Web), which states:

> "Finally, be aware that no set of guidelines will always accurately predict the success of a primer. Some primers may fail for no apparent reason, and primers that appear to be poor candidates may work well."

As indicated above, Makino et al. does not teach or suggest any *capB* primers or probes. In addition, the primers and/or probes disclosed by Ramisse et al., Wittwer et al., Qi et al., and Buck et al. are all directed toward non-*capB* sequences. On the other hand, the presently claimed primer and probe sequences exhibit a high sensitivity and specificity toward their targets.

Applicants respectfully refer the Examiner to Examples 1 and 4 of the specification, which discuss the sensitivity of the claimed primer and probe sequences, and to Example 5, which discusses the specificity of the claimed primer and probe sequences. In addition, each of the claimed probe sequences has a particular melting temperature, which can be used to confirm the presence or absence of *B. anthracis* in a sample. Therefore, the claimed probe sequences can be used to further increase the accuracy of detecting *B. anthracis*. See, for example, page 23, lines 5-7 and Example 3 of the specification.

Based on the current case law, the claimed primer and probe sequences are not obvious over the cited references. See, for example, *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992) ("[t]hat the claimed compound is a species of a genus disclosed in a prior art reference does not necessarily make the compound *prima facie* obvious") and *In re Bell*, 991, F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993) ("given the nearly infinite number of possibilities suggested by the prior art, and the failure of the cited prior art to suggest which of those possibilities [to select], the claimed sequences would not have been obvious"). Applicants submit that the Buck et al. reference is not relevant because, as indicated above, the results reported by Buck et al. using a single sequencing primer are not representative of results using pairs of primers and/or probes in various types of amplification reactions. In addition, the template nucleic acid sequenced by Buck et al. is not a *B. anthracis* nucleic acid.

The claimed primer and probe sequences are not obvious over the cited art. In view of the amendments and remarks herein, Applicants respectfully submit that the rejection of claims 33-35 under 35 U.S.C. §103 is moot, and should not be applied to new claims 57-69 and 96.

Claims 39-41 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ramisse et al., Wittwer et al., and Qi et al., further in view of Price et al. (*J. Bacteriol.*, 181:2358-62, 1999) and Buck et al. Applicants respectfully traverse this rejection.

With respect to the Examiner's statements on page 5 of the Office Action regarding claim interpretation, Applicants do not agree with the Examiner. To expedite prosecution, however, Applicants have canceled claims 32-47 without prejudice to continued prosecution and have submitted corresponding new claims 57-96. New claims 70-82 and claim 96 recite at least one *pagA* primer or probe sequence from original claims 39-41.

The Examiner asserted that the claimed *pagA* primers and probes are "structural homologs derived from sequences suggested by the prior art," and cited *In re Deuel* to support this assertion. The Examiner relied, in part, on Price et al., which compares *pagA* sequences, and Buck et al., which discloses that a number of different sequencing primers all were used successfully to sequence a particular target nucleic acid.

As with the capB sequences, the claimed *pagA* primers and probes are not "structural homologs" of the *pagA* sequence disclosed by Price et al. As indicated above, *In re Deuel* does not indicate that complementary sequences are "structural homologs," and, therefore, *In re Deuel* is not relevant to the pending claims reciting particular primer or probe sequences. Also as discussed above, Buck et al. is not relevant either. Applicants reiterate that we are aware of no case law standing for the proposition that a longer sequence makes *per se* obvious specific primer and probe sequences from within that longer sequence.

There is no suggestion by Price et al. to use the claimed primers and probes. Price et al. discloses *pagA* primers that all differ from the claimed primer and probe sequences, and the primers and/or probes disclosed by Ramisse et al., Wittwer et al., Qi et al., and Buck et al. are all directed toward non-*pagA* sequences. On the other hand, the claimed primer and probe sequences exhibit a high sensitivity and specificity toward their targets. As indicated above, Examples 1 and 4 of the specification discuss the sensitivity of the claimed primer and probe sequences, and Example 5 discusses the specificity of the claimed primer and probe sequences. Page 23, lines 5-7 and Example 3 of the specification discloses and discusses the melting temperature of each probe, which can be used to further increase the accuracy of detecting *B. anthracis*. Price et al. does not examine either the sensitivity or specificity of the disclosed primers, and Price et al. also does not use a method involving the melting point of a probe to increase reporting accuracy.

The claimed *pagA* primer and probe sequences are not obvious over the cited art. In view of the amendments and remarks herein, Applicants respectfully submit that the rejection of claims 39-41 under 35 U.S.C. §103 is moot, and should not be applied to new claims 70-82 and 96.

Claims 44-46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ramisse et al., Wittwer et al., and Qi et al., further in view of Bragg et al. (*Gene*, 81:45-54, 1989) and Buck et al. Applicants respectfully traverse this rejection.

With respect to the Examiner's statements on page 5 of the Office Action regarding claim interpretation, Applicants do not agree with the Examiner. To expedite prosecution, however, Applicants have canceled claims 32-47 without prejudice to continued prosecution and have submitted corresponding new claims 57-96. New claims 83-96 recite at least one particular *lef* primer or probe sequence from original claims 44-46.

The Examiner asserted that the claimed *lef* primers and probes are "structural homologs derived from sequences suggested by the prior art," and cited *In re Deuel* to support this assertion. The Examiner relied, in part, on Bragg et al., which discloses the sequence of the *lef* gene, and Buck et al., which discloses that a number of different sequencing primers all were used successfully to sequence a particular target nucleic acid.

As with the *capB* and *pagA* sequences, the claimed *lef* primers and probes are not "structural homologs" of the *lef* sequence disclosed by Bragg et al. As indicated above, *In re Deuel* does not indicate that complementary sequences are "structural homologs," and, therefore, *In re Deuel* is not relevant to the pending claims reciting particular primer or probe sequences. Also as discussed above, Buck et al. is not relevant. Applicants reiterate that we are aware of no case law standing for the proposition that a longer sequence makes *per se* obvious specific primer and probe sequences from within that longer sequence

There is no suggestion by Bragg et al. to use the claimed primers and probes. Bragg et al. used primers to sequence the *lef* gene, but Bragg et al. does not explicitly disclose the sequence of those primers. Additionally, the primers and/or probes disclosed by Ramisse et al., Wittwer et al., Qi et al., and Buck et al. are all directed toward non-*lef* sequences. On the other hand, the claimed primers and probes display a high sensitivity and specificity toward their targets. As indicated above, Examples 1 and 4 of the specification discuss the sensitivity of the claimed primer and probe sequences, and Example 5 discusses the specificity of the claimed primer and probe sequences. Page 23, lines 5-7 and Example 3 of the specification discloses and discusses the melting temperature of each probe, which can be used to further increase the accuracy of

detecting *B. anthracis*. Bragg et al. provide no information on the sensitivity or specificity of their primers, and no information on using melting temperature to increase reporting accuracy.

The claimed *lef* primer and probe sequences are not obvious over the cited art. In view of the amendments and remarks herein, Applicants respectfully submit that the rejection of claims 44-46 under 35 U.S.C. §103 is moot, and should not be applied to new claims 83-96.

CONCLUSION

Enclosed is a $938 check ($828 for excess claim fees and $110 for the Petition for One-Month Extension of Time). Please apply any other charges or credits to Deposit Account 06-1050.

Respectfully submitted,

Date: May 28, 2004

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